REMARKS

Applicants gratefully acknowledge the courtesy shown by the Examiner and Supervisory Examiner Yvonne Eyler during the interview on July 31, 2003. During the interview, the Examiners acknowledged that Applicants' arguments concerning the rejection for lack of written description had merit and consequently that claims 18 and the claims dependent thereon may in fact meet the written description requirement. In addition, Applicants representative presented a proposed claim drafted to address the concerns with respect to reciting functionality as well as structure, and this claim is submitted in the form of new claim 42. New claims 43-47 also address the concerns with respect to reciting functionality as well as structure and are submitted herewith.

The Examiner also acknowledged that claims 17, 28-30, 34-35, 38, and 39 were allowable, and the omission of this indication of allowability in the final Office Action was an oversight.

In the final Office Action, the Examiner maintained the rejection of claims 18, 31-33, 36, 37 and 40-41 under 35 U.S.C. §112, 1st paragraph. The grounds for rejecting independent claim 18 and the claims dependent thereon are substantially the same, and are accordingly are addressed here together.

The Examiner's basis for rejection was that the claims drawn to a "purified polypeptide comprising amino acids 1-45 of the sequence depicted in SEQ ID NO: 2" failed to recite intrinsic function provided by amino acids 1-45 of SEQ ID NO: 2, such as that an estrogen receptor-β with this sequence had a 2 to 3 greater stimulation of estrogen response element (ERE) activity, and was

capable of attenuating IL-1β mediated NF-kB activity while an estrogen receptor-β lacking this sequence did not have that activity.

At the interview, Applicants' representative noted that the claim was drawn to an estrogen receptor-β comprising amino acids 1-45 of the sequence depicted in SEQ ID NO: 2. Thus, the Examiner's rejection did not address the pending claim, which is to "an isolated estrogen receptor-β comprising amino acids 1-45 of the sequence depicted in Figure 4 SEQ ID NO: 2." As discussed at the interview, such a claim meets the written description requirement because it provides a structure or formula, the sequence of amino acids of amino acids of 1-45 SEQ ID NO: 2, and a chemical name, estrogen receptor-β. Indeed, the term "estrogen receptor" is well defined in the art and carries with it functionality as well as structure. Consequently, the claim provides " '...a precise definition, such as by structure, formula, [a]nd chemical name,' of the claimed subject matter *sufficient to distinguish it from other materials*." *Regents of the Univ. of Cal. v. Eli Lilly & Co.,* 119 F.2d. 1559, 1568, 43 USPQ2d 1398, 1405 (citing *Fiers v. Revel,* 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993); *In re Smythe,* 480 F.2d 1376, 1383, 178 USPQ 279, 284-285 (CCPA 1973).

In the Office Action, the Examiner stated that the peptide comprising amino acids 1-45 lacks "definitive structural features of the claimed genus of polypeptides and the claim fails to disclose the functional features of the genus polypeptides." (Office Action, p. 5). However, the amino acid sequence of amino acids 1-45 of SEQ ID NO:2 is unambiguously a definitive structural feature, and the claimed genus of estrogen receptor-β provides both structure and function as one of ordinary skill in the art would readily appreciate.

The contention further on in the Office Action that "[t]here is no description of the conserved regions which are critical to the structure and function of the genus claimed" (p. 5) seems to ignore

the abundant description in the specification of the functional features provided by that defined structure. In other words, where, as here, the applicants set forth a precise sequence (amino acids 1-45), and that their invention comprises polypeptides, particularly estrogen receptors, that comprise the sequence, there is no doubt that the inventors possessed such polypeptides, particularly estrogen receptors. Indeed, the Examiner's contention that "[s]tructural features that could distinguish the compounds in the genus from others are missing from the disclosure" (p. 5) is not correct, since, as acknowledged by the Examiner in the record and agreed at the interview, the sequence of amino acids 1-45 SEQ ID NO:2 is not in the prior art of record, and clearly distinguishes a polypeptide comprising that sequence from other polypeptides, particularly estrogen receptors.

The information relating structure to function is abundant in the specification, as the Examiner has noted. For example, on page 4 of the Office Action, the Examiner recites the characteristics of an estrogen receptor comprising the recited amino acid sequence in comparison to an estrogen receptor lacking the sequence: there is a 2-3 fold greater stimulation of the estrogen response element activity, and an estrogen receptor containing the 45 amino acid sequence was capable of attenuating IL-1β mediated NF-kB activity whereas the estrogen receptor lacking this sequence did not exhibit this inhibitory activity.

On page 13 of the specification, experimental results are provided showing that the full length estrogen receptor-β stimulated about 2-3 times more activity in the estrogen response element than the truncated form of the estrogen receptor. Specifically, "[t]he results shown in Figure 6A indicate that, in the presence of estradiol, hERβ_1 caused a 2-fold stimulation of ERE activity." (p. 13, ll. 3-4). "By contrast, hERβ_1 under the same conditions caused a 6-fold stimulation of ERE

activity" demonstrating that "hERβ_L is about 3-fold more active than hERβ_T in this situation" (p. 13, ll. 4-6).

In addition, the experimental results detailed in the specification show that full length estrogen receptor β attenuated IL-1β-mediated NF-kB activation while the shorter form of estrogen receptor did not. Specifically, "the results shown in Figure 7 indicate that hERβ_L was capable of attenuating IL-1β-mediated NF-kB transcriptional activation (to an extent similar to that observed with hERα), while hERβ_T exhibited no inhibitory activity" (p. 13, ll. 10-13).

In yet another example relating structure to function, "[t]he results shown in Figure 8 indicate that hERβ_L is 2-3 times more active than hERβ_T in activating the ERE-reporter gene in the presence of estradiol" (p. 13, ll. 19-20).

As discussed during the interview, Applicants are submitting herewith proposed new claims 42-48 which recite the characteristics of the 1-45 sequence of the invention when combined with the human estrogen receptor-β.

As discussed at the interview, having provided the sequence as recited in the claims, and demonstrated that the sequence has a role to play in estrogen receptor functionality, Applicants have established possession of the claimed subject matter. Therefore, their claims are entitled to broadly cover any polypeptide, and certainly any estrogen receptor, that comprises the sequence. The sequence can indeed act as a handle for antibody binding, which may be useful in purification or for targeted suppression of estrogen receptors in model systems. Thus, as discussed at the interview, it is not necessary for all of the utilities of the 45 residue amino sequence component of the claimed

polypeptide to demonstrate the same functionality it has with respect to human estrogen β when found at the end terminus of human estrogen receptor-β.

In summary, the estrogen receptor-β comprising the unique 45 amino acid N-terminal sequence recited in claim 18, claims dependent thereon, and claims 45-47, and the polypeptide comprising the 45 amino acids sequence which imparts its specific functional activity as recited in claims 42-44; meet the written description requirement. Maintaining otherwise unfairly denies Applicants the value of their invention an indeed is contrary to established law with respect to written description, particularly in the context of biotechnological inventions. *See Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

CONCLUSION

Applicants respectfully request the Examiner enter the foregoing amendment and the remarks in the file history of this application. Based on the interview, and the remarks presented here, Applicants believe that the claims meet the written description requirement. Accordingly, allowance of the claims is earnestly solicited.

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Respectfully submitted,

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